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(19)

(54) PRODUCTION OF MULTICOMPONENT DIET SUPPLEMENTS

(71) We, MERCK & CO INC, a corporation duly organised and existing under the laws of the State of New Jersey, United States of America, of Rahway, New Jersey, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention is concerned with mixed dietary supplements.

The state of the art of blending mixtures of vitamins and blending vitamins with minerals includes methods of mixing, careful matching of constituent ingredient particle sizes, consideration of specific gravity differences among ingredients and sequences such as mix-mill-mix. These are time and labor consuming procedures. Classification of particles in shipping and handling is a constant difficulty.

Attempts have been made in prior practices to solve the problem of tablet strength by granulating vitamin and/or mineral particles. Typical binders used for this purpose in the past include solutions of glucose, gum Arabic, gelatin, sucrose, starch, water, alcohol, methylcellulose, and shellac. Such procedures and ingredients lead to granules that can be tableted. Reproducibility is poor, however, in fluidity of particles and mechanical strength of the tablets. Also discoloration of the vitamin and minerals sometimes results.

In the past, as shown by U.S. Patent No. 3265629, more than one substance has been enclosed in a single enveloping wall but those substances are joined or attached to each other by a spraying operation so that the wall must surround the adhering substances. It has now been found that this is unnecessary.

In accordance with the present invention, there is provided a method of microencapsulating a mixture of discrete particles of dietary supplement materials, the particles being less than 100 microns in size, while maintaining the uniformity of the mixture, that comprises mixing together 100 parts by weight of a solvent for ethylcellulose in which the said materials are insoluble, 1 to 5 parts by weight of ethylcellulose having a 45 to 50% ethoxyl content and a viscosity of 95 to 100 centipoises, and 1 to 50 parts by weight of the said mixture of particles; heating the resulting mixture of solvent, ethylcellulose and particles to a temperature not exceeding the boiling point of the solvent; allowing the system to cool with continued stirring whereby the ethylcellulose forms microcapsules each of which contains discrete particles of the said materials in substantially the same proportions as in the original mixture, and separating and recovering the said microcapsules.

The invention also provides a mixture of discrete particles of dietary supplement materials microencapsulated in ethylcellulose or in a mixture of ethylcellulose and polyethylene, each microcapsule containing substantially the same blend of the said materials as each other microcapsule. It will be seen that when proceeding in accordance with the present invention, the nutrient particles are used as separate, discrete, unattached fragments and they are enclosed as such by the microencapsulating wall.

The present invention involves the microencapsulation of mixtures by the known arts of polymer/polymer incompatibility coacervation and film formation from polymer solution by loss of solvent as embodied in United States Patent Nos. 2800457, 3106308, 3155590 and 3495988, and British Patent Nos. 965070, 10112658, and 1016839. Other microencapsulation processes which may be used are disclosed in Netherlands Patent No. 6611661, French Patent No. 1453745, and U.S. Patent No. 3531418.

In a preferred embodiment of the present invention, the system also comprises polyethylene having a molecular weight of from 5000 to 10000 (an average of 7000 is preferred) and from 1 to 5 parts by weight of it should be added per 100 parts by weight

of the solvent. In this case the solvent chosen must also dissolve polyethylene.

Suitable solvents for the coating solution, whether or not polyethylene is used, include cyclohexane and hexane. The ethylcellulose should preferably have a 47.5% ethoxyl content and a 100 cps. viscosity but a range of 45.0—50% ethoxyl content and a 95—110 cps. viscosity is permissible. The viscosity is measured at 25°C. as a 5% by weight solution in a 80:20 toluene-ethanol mixture. On the basis of 100 grams of cyclohexane, there is added 1 to 5 grams of the ethylcellulose to thereby vary the thickness of the encapsulating film.

The microcapsules of this invention have important use in making multivitamin-mineral tablets. The previously known vitamin-mineral mixes used for making compressed tablets lack certain properties necessary for getting a desirable product. The mechanical strength of the tablet is low. The flow rate of the mixture from the hopper to the tableting die can be so erratic that some die holes may not fill properly. At least the preferred products of the present invention have improved uniformity of flow and produce a tablet that has high mechanical strength but still releases its active material.

These vitamin-mineral blends are also used in the food industry to fortify baked goods, for instance, and as coatings on breakfast cereals. In such uses it is important that granular, crystalline and/or powder-textured blends of vitamins and/or minerals be uniform from one portion of a batch to another, and from batch to batch. It is equally important to avoid "classification" or stratification of constituents of the blend as the blend is unloaded from production machinery, during packaging, shipping and other handling.

The particles of dietary supplement materials suitable for blending together in accordance with the present invention include water-soluble vitamins such as ascorbic acid, folacin, niacin, riboflavin, thiamine, vitamins of the B_6 complex such as pyridoxine, vitamin B_{12}, and esters, salts and amines thereof, and minerals such as those containing calcium, phosphorus, iodine, iron and magnesium. Preferred mixtures contain two or more of the following: niacin, riboflavin, thiamine, ascorbic acid, pyridoxine, vitamin B_{12} and iron. Among particularly preferred combinations of dietary supplement materials are the following: niacin, riboflavin and thiamine, with or without ascorbic acid and/or iron, and niacin, riboflavin, thiamine, pyridoxine and vitamin B_{12}, with or without ascorbic acid. The individual ingredients may be replaced by their salts, esters or amides, where these are formed and are suitable.

The materials should be present in multi-vitamin-mineral preparations in the following daily dosage ranges:

Substance	Amount
ascorbic acid	25—75 mg
folacin	0.01—1 mg
niacin	0.1 — 2.5 mg
riboflavin	0.1 — 2.5 mg
thiamine	2—25 mg
vitamin B_6	0.1 —3 mg
vitamin B_{12}	0.1 —10.0 μg
calcium	0.1 — 2.0 g
phosphorus	0.1 — 2.0 g
iodine	10—200 μg
iron	5—50 mg
magnesium	25—500 mg

These particles are preferably micro-atomized so that 98% of them are under 50 microns in size. The particles can be up to 100 microns in size and some of them in the 50 to 100 micron range will be individually encapsulated but some of them will be trapped with other particles in a single capsule. Particles above 100 microns in size will almost all be individually microcapsulated. The different ingredients can each have quite a different size below 100 microns and preferably below 50 microns as the polymer solution tends to equally suspend them all in a uniform distribution until the microencapsulation traps them in this uniform blend.

During the cooling step the ethylcellulose starts to form an encapsulating wall around minute agglomerates or clumps of the ingredients while they maintain substantially their original blended ratio. In many of the microcapsules the relative ratio of the individual ingredients will be exactly that of the original mixture and in any event several of the microcapsules when randomly grouped together will have a composite ratio which corresponds to the original overall mixture ratio.

Representative examples are the following. The words 'Merpress', 'Stabicate', 'Cab-o-Sil', 'Auical' and 'Syloid' are trade marks and mesh sizes are U.S. standards.

EXAMPLE 1

The following were dispersed in 300 gm. cyclohexane, using an upthrust turbine impellor.

- 6 gm. Ethylcellulose (47.5% ethoxyl content by weight, viscosity 100 cps. as 5% solution in 80:20 toluene: ethanol at 25°C.
- 6 gm. Polyethylene granules (molecular weight about 7000).
- 44.1 gm. Niacinamide (325 mesh).
- 5.5 gm. Riboflavin (325 mesh).
- 4.4 gm. Thiamine mononitrate (325 mesh).

Stir the system with heating. At 80°C. both the ethylcellulose and the polyethylene had dissolved in the cyclohexane.

Stirring was continued while the system was allowed to cool. As the temperature dropped, solvated ethylcellulose developed as a separate phase due to the presence of the polyethylene. The solvated polyethylene, distributed in the cyclohexane as droplets by the turbine, tended to wet small clumps of vitamin mix and to envelop them. As the temperature dropped further, the ethylcellulose lost solvent and developed into solid encapsulating walls. The continuous phase, cyclohexane, contained minute particles of polyethylene. At 45°C. the walls had stopped building up. Cold cyclohexane was added to reduce the temperature still further. The supernatant cyclohexane was poured off together with the minute particles of polyethylene. The microcapsules were resuspended in clean cyclohexane. Removal from and suspension in cyclohexane was repeated as necessary until the capsules were washed clean of polyethylene and other debris. The capsules were spread to dry. The resultant capsules with a 90% vitamin content, when screened through standard Taylor sieves, had the following size distribution (wt.%):

+20 mesh	3.2
−20/+35	5.4
−35/+80	71.9
−80/+100	8.1
−100	11.4

The ratio by weight of vitamins processed was 1.00 niacinamide: 0.12 riboflavin: 0.10 thiamine mononitrate. The ratio of vitamins determined in 2 grams sample of microcapsules was 1.00: 0.12: 0.10.

Niacinamide and thiamine are bitter. Laboratory personnel found no bitter taste when they put several capsules on the tongue and swallowed them.

EXAMPLE 2

Capsules were prepared successfully as in Example 1, but the following were dispersed in 300 gm. cyclohexane, in addition to the 6 gm. Ethylcellulose (this becomes the external phase, or capsule wall) and the 6 gm. polyethylene:

- 3.3 gm. Thiamine mononitrate (325 mesh)
- 3.3 gm. Riboflavin (325 mesh)
- 1.6 gm. Pyridoxine hydrochloride (325 mesh)
- 32.9 gm. Niacinamide (325 mesh)
- 68.9 gm. Sodium ascorbate (325 mesh)

The above nutrients become the internal phase, or encapsulated material.

The resultant capsules with a 95% vitamin content, when screened through standard Taylor sieves, had the following size distribution (wt.%):

+12 mesh	0.19
−12/+20	0.47
−20/+60	30.59
−60/+80	49.20
−80/+100	10.83
−100/+200	8.72
−200	Trace

EXAMPLE 3

Capsules were prepared successfully as in Example 1, but the following internal phase was used:

- 26 gm. Thiamine mononitrate
- 21 gm. Riboflavin
- 21 gm. Pyridoxine hydrochloride
- 37 gm. Niacinamide

The resultant capsules with a 95% vitamin content, when screened through standard Taylor sieves, had the following size distribution (wt.%):

+12 mesh	0.4
−12/+16	3.4
−16/+20	1.7
−20/+30	1.4
−30/+40	0.9
−40/+60	2.0
−60/+80	3.7
−80/+100	15.4
−100/+140	37.9
−140/+200	29.3
−200/+325	3.6
−325	0.3

EXAMPLE 4

Capsules were prepared successfully as in Example 1, but the following internal phase was used:

- 3.3 g. Thiamine mononitrate
- 3.3 g. Riboflavin
- 1.6 g. Pyridoxine hydrochloride
- 32.9 g. Niacinamide
- 68.9 g. Sodium ascorbate
- 1.65 g. Cobalamine Concentrate Type S 100. (This is crystalline Vitamin B_{12} diluted 100 μg/gm. with mannitol).

The resultant capsules had an internal phase content of 95%. This formulation was of particular interest because of the small amount of Vitamin B_{12} in the blend. This is a good measure of the efficiency of the distribution of ingredients. The theoretical quantity of B_{12} in the capsules was 0.014 mg./gm. capsules. The amount found was 0.012 mg./gm.

EXAMPLE 5

An 8" diameter stainless steel kettle, with 4 baffles was charged with 1500 gm. cyclo-

hexane, 30 gm. ethylcellulose (of the type described in Example 1), and 30 gm. polyethylene (of the type described in Example 1). The system was stirred at 220 rpm with a 2" diameter turbine impellor, heating to 78°C. At 78°C. the following blend was added:

4.34 g. Riboflavin
7.17 g. Thiamine hydrochloride
51.70 g. Niacinamide
486.80 g. Ferrous sulphate dried.

The system was allowed to cool to 45°C., and processed further as in Example 1. The resultant capsules had an internal phase content of 95%, and a Taylor sieve analysis (wt.%) as follows:

+12 = 0.24
−12/+30 = 1.47
−30/+42 = 2.62
−42/+100=30.80
−100/+150=37.30
−150/+200=18.90
−200 = 8.60

Note that the ingredients include ferrous sulfate, a nutrient that is not a vitamin. These are multi-component capsules. The term multi-component is used as distinct from multi-vitamin.

EXAMPLE 6

The −40/+100 mesh fraction of microcapsules prepared in Example 5 were compressed on a Manesty Beta Press using 10/32" S.C. punches. No lubricant, excipient or binder were added to the microcapsules.

Resultant tablets weighed 200 mg. and had a Strong-Cobb hardness of 22.0 kg. Friability (Wollish Friabilator) loss in 4 minutes was 0.002 gm; in 30 minutes, 0.007 gm.

Tablets prepared with the −100/+150 mesh fractions had a hardness of 21.8 kg., weight 200 mg., and a friability loss in 30 minutes of 0.0266 grams.

Tablets prepared with the −200 mesh fraction had a weight of 199 mg., a hardness of 22.3 kg. and friability loss in 30 minutes of 0.0218 gram.

These tablets agitated in simulated gastric fluid at 37°C. would release 35% of the internal phase in one hour and the balance during the second hour.

This example demonstrates an ultimate in direct compressibility. Not one ingredient had to be added to the multi-ingredient microcapsules. The resultant capsules demonstrated good hardness and very low friability.

EXAMPLE 7

The −35/+80 mesh fraction of microcapsules prepared in Example 1 were included in a commercial multivitamin-mineral preparation having the composition:

Microcapsules of Example 1	1,006.8	gm.
Vitamin A/D_2 500 μ/50 μ	100.0	gm.
Vitamin A Acetate	450.0	gm.
*Thiamine Mononitrate	36.5	gm.
*Riboflavin	12.4	gm.
Merpress (Niacinamide: ascorbic acid, 1:3)	1,006.8	gm.
Sodium ascorbate	1.530.0	gm.
Calcium pantothenate	250.0	gm.
Pyridoxine hydrochloride	60.0	gm.
Stabicote (Vit. B_{12}, 1% in gelatin)	6.25	gm.
Vitamin E Acid Succinate	136.5	gm.
Carnauba (Wax (−100 mesh)	240.0	gm.
Avicel	317.5	gm.
Syloid, Grade 68	27.0	gm.
Stearic Acid	72.5	gm.
Magnesium Stearate	20.0	gm.

*These were added in addition to the amounts included in the microcapsules, to raise the quantities to the precise amount called for in the formula

The above blend was compressed in a Manesty Beta Press, run at 1000 tablets/minute using a No. 1 capsule shaped punch.

The resultant tablets average 550.5 mg. each and had a thickness of 0.225". They had a very good whiteness. Flow from the hopper to the punch was far superior to a blend containing no microencapsulated material. Strong-Cobb hardness of the tablets was 22.0 kg. Without microencapsulated material in the blend the Strong-Cobb hardness would be 16—18 kg.

EXAMPLE 8

Microcapsules of Example 2 were included in a commercial multivitamin-mineral preparation having the composition:

Microcapsules of Example 2	2,570.0	gm.
Vitamin A/D_2 500 μ/50 μ	100.0	gm.
Vitamin A Acetate	450.0	gm.
*Thiamine Mononitrate	36.3	gm.
*Riboflavin	32.55	gm.
Merpress	1,240.0	gm.
*Niacinamide	11.1	gm.
Calcium Pantothenate	250.0	gm.
*Pyridoxine Hydrochloride	24.6	gm.
Stabicote 1%	6.25	gm.
Vitamin E Acid Succinate	136.5	gm.
Carnauba Wax (C-100 mesh)	240.0	gm.
Avicel	317.5	gm.
Syloid, Grade 68	27.0	gm.
Stearic Acid	75.25	gm.
Magnesium Stearate	20.0	gm.

*These were added over and above that included in the microcapsules, to raise the quantities to the precise amount called for in the formula.

The above blend was compressed as in Example 6. The flowability into the dies was more uniform than when the microcapsules were not included. The resultant tablets averaged 555.7 mg. each, had a thickness of 0.220", and a Strong-Cobb hardness of 21.8 kg. This hardness compares favorably with 16—18 kg. that would be expected in a similar blend without microencapsulated material.

EXAMPLE 9

Microcapsules of Example 3 were included in a typical daily vitamin preparation:

Microcapsules of Example 3	21.0 gm.
Cyanocobalamine 0.1% in gelatin	4.4 gm.
Merpress	146.6 gm.
Calcium Pantothenate	10.0 gm.
Magnesium Stearate	6.0 gm.
Cab-O-Sil	2.0 gm.
Vitamin A/D 500/50	27.0 gm.
Spray Dried Lactose	81.5 gm.
Avicel	81.5 gm.

Tablets were prepared by direct compression, using a 10/32" deep cup. Resultant tablets averaged 191 mg. and had a Strong-Cobb hardness of 7.2 kg. A comparable preparation with no microencapsulated ingredient would have a hardness of 5 or 6 kg.

EXAMPLE 10

An 8" diameter stainless steel kettle, with 4 baffles was charged with:

5 litres Cyclohexane
36 gm. Riboflavin, (325 mesh)
36 gm. Thiamine mononitrate (200 mesh)
428 gm. Niacinamide (200 mesh)
120 gm. Ethylcellulose (as in Example 1)

The system was stirred at 450 rpm with a 3" turbine impellor, located 1½" from the bottom of the kettle, heating to 78°C. At 80°C. the ethylcellulose had dissolved in the cyclohexane.

Stirring was continued while the system was allowed to cool. As the temperature dropped, solvated ethylcellulose developed as a separate phase due to the poor solvent quality of cyclohexane at lower temperatures. The solvated ethylcellulose distributed in the cyclohexane as droplets by the turbine, tended to wet small clumps of vitamin mix and to envelop them. As the temperature dropped further, the ethylcellulose lost solvent and developed into solid encapsulating walls. At 55°C. the walls had stopped building up. Cold cyclohexane (1 liter) was added to reduce the temperature still further.

The supernatant cyclohexane was poured off. The capsules were dried in a Glatt fluid bed dryer of 5 kilogram capacity.

The resultant capsules were in the 50 μ range and had a content as follows:

Riboflavin	5.8%
Thiamine Mononitrate	5.8%
Niacinamide	69.0%
Ethylcellulose	19.4%

Riboflavin, thiamine and niacinamide are bitter. Laboratory personnel found the vitamins to be taste masked when they put several capsules on the tongue and swallowed them.

EXAMPLE 11

Capsules were prepared successfully as in Example 10, but the system was stirred at 300 rpm. The resultant capsules were in the 100—200 μ range.

EXAMPLE 12

Capsules were prepared successfully as in Example 11, but the internal phase consisted of:

9 gm. Riboflavin
9 gm. Thiamine mononitrate
111 gm. Niacinamide
371 gm. Ascorbic Acid (200 mesh)

The resultant capsules were in the 100—200 μ range and had a content as follows:

Riboflavin	1.5%
Thiamine mononitrate	1.5%
Niacinamide	17.9%
Ascorbic Acid	59.8%
Ethylcellulose	19.4%

EXAMPLE 13

Microcapsules were prepared successfully as in Example 10, but the internal phase consisted of:

20 gm. Riboflavin
20 gm. Thiamine mononitrate
240 gm. Niacinamide
800 gm. Ascorbic Acid

The system was stirred at 400 rpm. The resultant capsules were in the 100—200 μ range and had a content as follows:

Riboflavin	1.7%
Thiamine mononitrate	1.7%
Niacinamide	20.0%
Ascorbic Acid	66.7%
Ethylcellulose	10.0%

EXAMPLE 14

Microcapsules were prepared successfully as in Example 10, but the internal phase consisted of:

12.6 gm. Riboflavin
12.6 gm. Thiamine mononitrate
151.1 gm. Niacinamide
503.7 gm. Ascorbic Acid

The system was stirred at 340 rpm. The resultant microcapsules were in the 100—200 μ range and had a content as follows:

Riboflavin	1.6%
Thiamine mononitrate	1.6%
Niacinamide	18.9%
Ascorbic Acid	62.9%
Ethylcellulose	15.0%

EXAMPLE 15

Capsules were prepared successfully as in Example 12, but scaled up to a 30 litre kettle, using a 4 inch turbine impellor, and stirring at 950 rpm. The charge to the kettle was:

18.75 liters Cyclohexane
34 gm. Riboflavin
34 gm. Thiamine mononitrate
416 gm. Niacinamide
1391 gm. Ascorbic Acid
450 gm. Ethylcellulose

The resultant microcapsules were in the 100—200 μ range and had a content as follows:

Riboflavin	1.5%
Thiamine mononitrate	1.5%
Niacinamide	17.9%
Ascorbic Acid	59.8%
Ethylcellulose	19.3%

EXAMPLE 16

Capsules were prepared successfully as in Example 10, but the kettle was charged with:

4 liters Cyclohexane
60.0 gm. Ethylcellulose
690.9 gm. Ascorbic Acid
230.3 gm. Niacinamide
23.0 gm. Riboflavin
28.6 gm. Thiamine mononitrate
35.0 gm. Pyridoxine hydrochloride
92.2 gm. Vitamin B_{12} with mannitol (0.1% active)

stir at 300 rpm.

The resultant capsules, in the 100—200 μ range had the following content:

Ethylcellulose	5.2%
Ascorbic acid	59.6%
Niacinamide	19.9%
Riboflavin	2.0%
Thiamine mononitrate	2.5%
Pyridoxine hydrochloride	3.0%
Vitamin B_{12}	0.008%

EXAMPLE 17

83.5 mg of microcapsules from Example 12 were combined with 414.0 gm. of a blend of microcrystalline cellulose and corn starch, and 2.5 gm. calcium stearate. The blend was screened through a 20 mesh sieve, and compressed at 500 mg., using a Manesty single punch 16/32 F. F.—B. E. open single score.

The resultant tablets were chewable. Laboratory personnel found the vitamins to be taste-masked.

EXAMPLE 18

Microcapsules were prepared successfully as in Example 5, but no polyethylene was used.

The resultant microcapsules were in the 100—200 μ range and had a content as follows:

Riboflavin	0.75%
Thiamine hydrochloride	1.24%
Niacinamide	8.191%
Iron (as ferrous sulfate)	26.50%
Ethylcellulose	5.16%

EXAMPLE 19

Microcapsules were prepared successfully as in Example 18, but by the following procedure:

1. Hardware:

30-Liter fermentation kettle, glass 12" diameter, 17" high.

Six-bladed down thrust turbine, 5" diameter, 1½" from bottom of kettle.

Four baffles, stainless steel, 1" wide.

Air-drive turbine.

Stainless steel tubing, coiled, for heating and cooling.

2. Disperse in 18.75 liters cyclohexane:

900 gm. Ethylcellulose (as in Example 1—18, but only 45 cps viscosity)
2539 gm. Ascorbic Acid
1691 gm. Niacinamide
405 gm. Riboflavin
461 gm. Thiamine Mononitrate

3. Stirring at a shaft speed of 2700 rpm, put steam through the coils to heat to 78°—80°C.

4. Stop heating. Pass cold water through coils, cooling the system to 35°C in one hour.

Resultant microcapsules had a content as follows:

the microcapsules should be added at as late a stage as possible.

WHAT WE CLAIM IS:—

1. A method of microencapsulating a mixture of discrete particles of dietary supplement materials, the particles being less than 100 microns in size, while maintaining the uniformity of the mixture, that comprises mixing together 100 parts by weight of a solvent for ethylcellulose in which the said materials are insoluble, 1 to 5 parts by weight of ethylcellulose having a 45 to 50% ethoxyl content and a viscosity of 95 to 110 centipoises, and 1 to 50 parts by weight of the said mixture of particles; heating the resulting mixture of solvent, ethylcellulose and particles to a temperature not exceeding the boiling point of the solvent; allowing the system to cool with continued stirring whereby the ethylcellulose forms microcapsules each of which contains discrete particles of the said materials in substantially the same proportions as in the original mixture, and separating and recovering the said microcapsules.

2. A method as claimed in claim 1 in which the dietary supplement materials include one or more vitamins or minerals.

3. A method as claimed in claim 1 or 2 in which the solvent is cyclohexane and the said temperature is about 80°C.

4. A method as claimed in claim 1 or 2 in which the solvent is hexane.

5. A method as claimed in claim 1 or 2 in which the solvent is a mixture of hexane and cyclohexane.

6. A method according to any one of claims 1 to 5 in which the ethylcellulose has an ethoxyl content of 47.5% and a viscosity of 100 cps.

7. A method as claimed in any one of claims 1 to 6 in which the original system further comprises 1 to 5 parts by weight of polyethylene having a molecular weight of 5000 to 10000 and the said solvent is one that is capable of dissolving polyethylene and ethylcellulose.

8. A method as claimed in claim 7 in which the polyethylene has a molecular weight of about 7000.

9. A method as claimed in any preceding claim in which from 10 to 40 parts by weight of the said discrete particles are used.

10. A method as claimed in any preceding claim in which the said discrete particles are added after the ethylcellulose has been brought into solution in the solvent.

11. A method as claimed in any preceding claim in which the said discrete particles are substantially all less than 50 microns in size.

12. A method as claimed in any preceding claim including the further step of compressing the microcapsules to form a tablet.

13. A mixture of discrete particles of dietary supplement materials microencapsulated in ethylcellulose or in a mixture of ethylcellulose and polyethylene, each microcapsule containing substantially the same blend of the said materials as each other microcapsule.

14. A microencapsulated mixture as claimed in claim 13 in which the dietary supplement materials are niacin, riboflavin and thiamine or salts, esters, or amides thereof.

15. A mixture as claimed in claim 14 in which the dietary supplement materials also include ascorbic acid or an ester, salt or amide thereof.

16. A mixture as claimed in claim 14 in which the dietary supplement materials also include iron or a salt thereof.

17. A mixture as claimed in claim 14 in which the dietary supplement materials also include pyridoxine and vitamin B_{12}.

18. A mixture as claimed in claim 15 in which the dietary supplement materials also include pyridoxine and vitamin B_{12}.

19. A mixture as claimed in claim 13 in which the dietary supplement materials is a mixture of two or more of the following, viz niacin, riboflavin, thiamine, ascorbic acid, pyridoxine, vitamin B_{12} and iron, and esters, salts, and amides thereof.

20. A mixture as claimed in claim 13 substantially as hereinbefore described in any one of the examples.

21. A compressed tablet containing a mixture as claimed in any one of claims 13—20.

22. A fortified edible food containing a mixture as claimed in any one of claims 13—20.

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